REMARKS

In a Rule 312 Amendment After Allowance filed via facsimile on August 17, 1999, claims 2, 4, 8 and 9 were amended and new claims 18-27 were added. Accordingly, claims 2-16 and 18-27 would have been pending upon entry of the August 17, 1999 Rule 312 Amendment After Allowance. In a February 22, 2000 voice mail message to Peter C. Lauro, Esq., attorney of record, Examiner Solola indicated that claims 10 and 27 would not be entered. The Examiner suggested that 18-26 be rewritten to depend from claim 10, or that alternatively claim 10 be cancelled.

Accordingly, claims 10 and 27 have been cancelled without prejudice. No new matter has been added.

Applicant submits that the foregoing cancellation of claims 10 and 27 does not require substantive examination by the Examiner. Accordingly, Applicant respectfully requests that this Amendment be entered. For the Examiner's convenience, the allowed claims together and the claims presented in the August 17, 1999 Rule 312 Amendment After Allowance, with claims 10 and 27 cancelled as set fort herein, are attached hereto as Appendix A.

Respectfully submitted,

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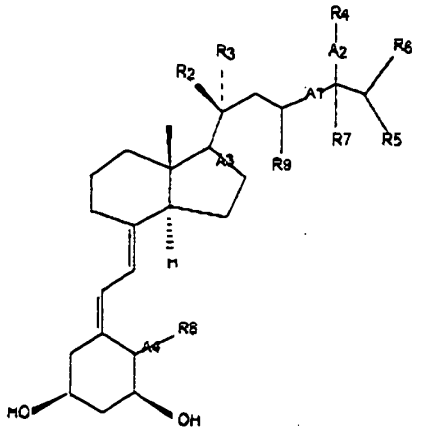
Date: February 23, 2000

APPENDIX A

2. An isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:

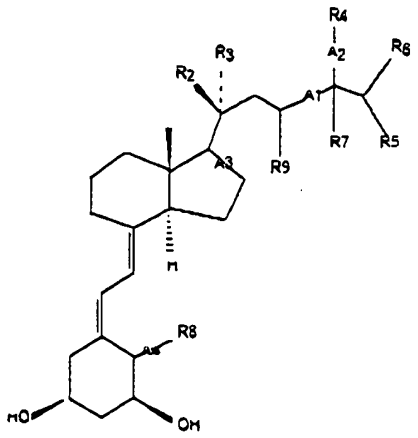


II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

3. The compound of claim 2, which is 1α(OH) vitamin D3, 1α,24 dihydroxy 3-epi vitamin D_3, 1α hydroxy 24-ethyl 3-epi vitamin D_3, 1α hydroxy 24-methyl 3-epi vitamin D_3, or 1α, 24-dihydroxy 24-methyl 3-epi vitamin D_3.

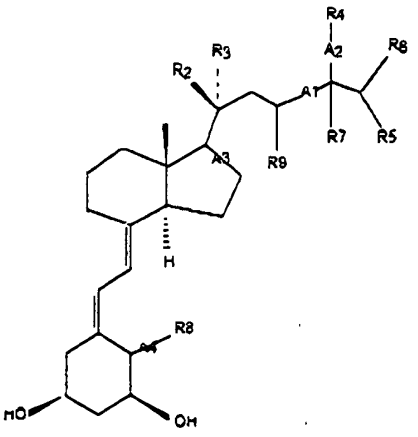
4. A method of treating a disorder characterized by an aberrant activity of a vitamin D_3-responsive cell, comprising administering to a subject an effective amount of a vitamin D_3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl, such that the aberrant activity of the vitamin D_3-responsive cell is reduced.

5. A method of treating a disorder characterized by an aberrant activity of a hyperproliferative skin cell, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



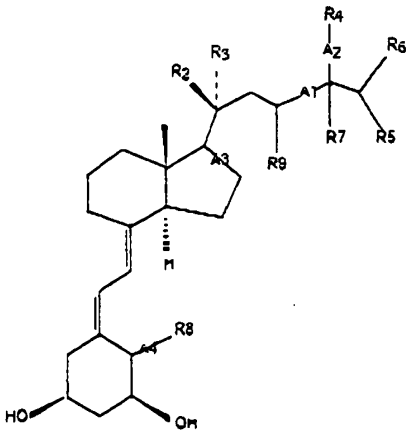
II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl, such that the aberrant activity of the hyperproliferative skin cell is reduced.

6. The method of claim 4, wherein the disorder comprises an aberrant activity of an endocrine cell.

7. The method of claim 6, wherein the endocrine cell is a parathyroid cell and the aberrant activity is processing and/or secretion of parathyroid hormone.

8. A method of treating secondary hyperparathyroidism, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:

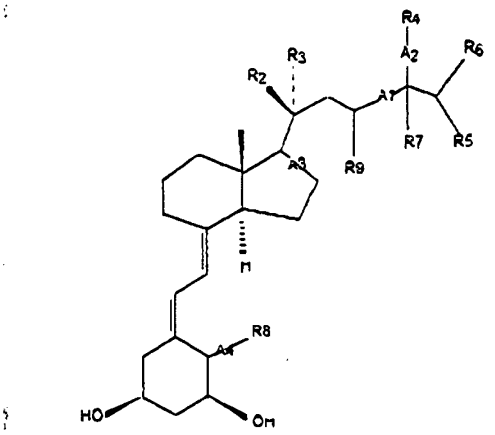


II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a

hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

9. A method of treating a disorder characterized by an aberrant activity of a bone cell, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl, such that the aberrant activity of the bone cell is reduced.

11. The method of claim 4, wherein the subject is a mammal.

12. The method of claim 11, wherein the mammal is a human.

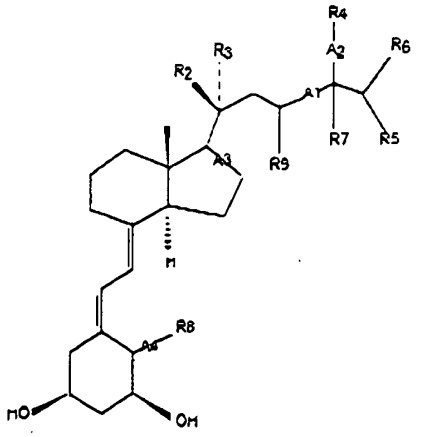
13. A method of ameliorating a deregulation of calcium and phosphate metabolism, comprising administering to a subject a therapeutically effective amount of a 3-epi vitamin D_3 compound of any of claims 2 or 3, so as to ameliorate the deregulation of the calcium and phosphate metabolism.

14. The method of claim 13, wherein the deregulation of the calcium and phosphate metabolism leads to osteoporosis.

15. A pharmaceutical composition comprising, a therapeutically effective amount of a vitamin D_3 compound of claim 2, and a pharmaceutically acceptable carrier.

16. The composition of claim 15, which is suitable for topical or oral administration.

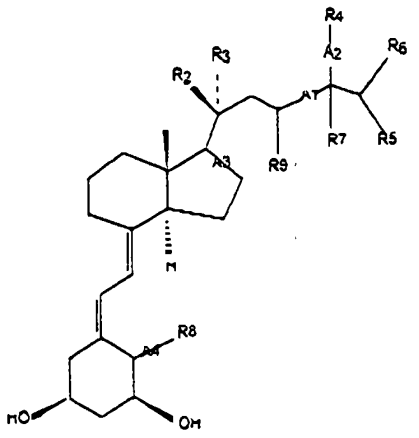
18. A method of treating osteoporosis, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

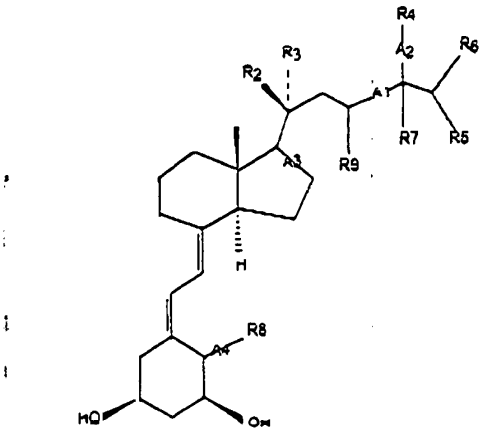
19. A method of treating osteodystrophy, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

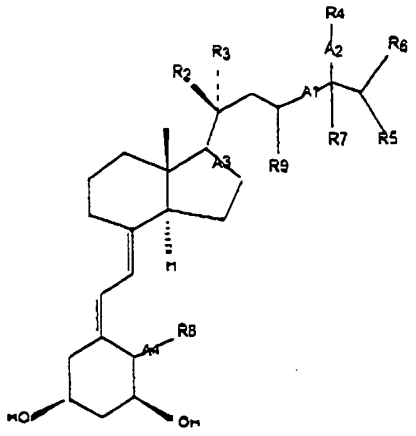
20. A method of treating senile osteoporosis, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

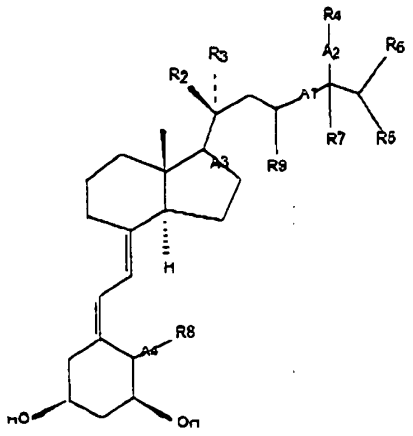
21. A method of treating osteomalacia, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

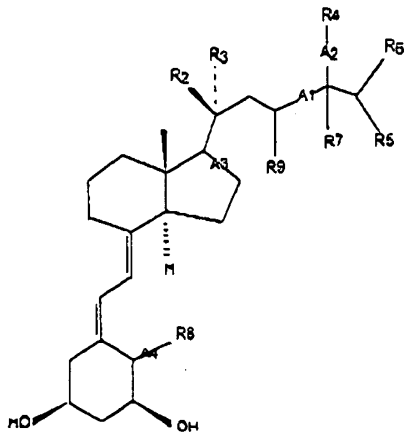
22. A method of treating rickets, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

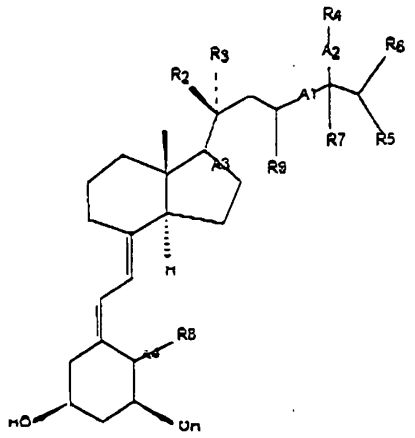
23. A method of treating osteitis fibrosa cystica, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

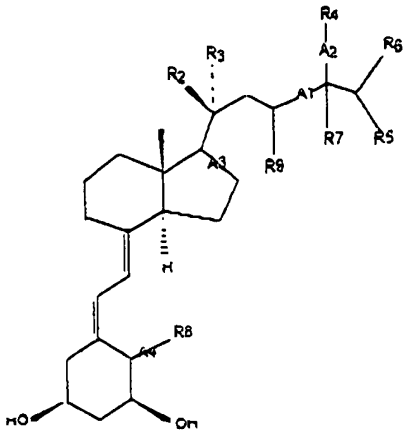
24. A method of treating renal osteodystrophy, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

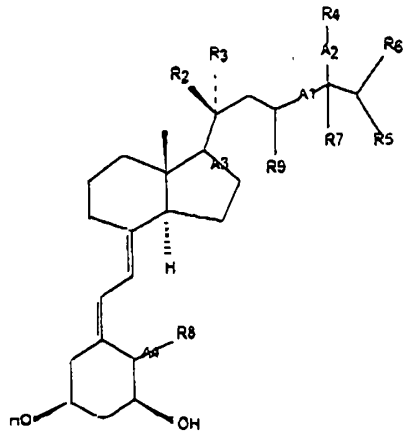
25. A method of treating cirrhosis, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.

26. A method of treating chronic renal disease, comprising administering to a subject an effective amount of an isolated 3-epi form of a 1α-hydroxy-vitamin D3 compound having formula II as follows:



II

wherein A_1 is a single, a double, or a triple bond; A_2, A_3 and A4 are each independently selected from the group consisting of a single or a double bond; R_2, R_3, R_4, R_7, R_8 and R_9 are independently selected from the group consisting of a hydrogen, a deuterium, a deuteroalkyl, a hydroxy, an alkyl, an alkoxide, an O-acyl, a halogen, a haloalkyl, a hydroxyalkyl, an amine or a thiol group, and wherein the pairs of R_2 and R_3, and R_4 and R_7 taken together are an oxygen atom; and R_5 and R_6 are independently selected from the group consisting of a hydrogen, a deuterium, a halogen, an alkyl, a hydroxyalkyl, a haloalkyl, and a deuteroalkyl.